REMARKS/ARGUMENTS

Claims 16, 19, and 59 have been revised to emphasize the nature of the claimed invention as featuring an antibody, or fragment thereof, that *both* binds the EA1 polypeptide of *B. anthracis and* is specific for the spores or vegetative cells of *B. anthracis*. Specificity for *B. anthracis* has always been a feature of the invention, and the inherent specificity of the antibodies is now expressly detailed in relation to *B. cereus*, *B. globigii*, and *B. licheniformis* in addition to *B. thuringiensis*. Support for the inherent specificity relative to *B. cereus* is found at least on page 3, lines 20-21, of the instant application. Support for the inherent specificity relative to the other *Bacilli* is found at least on page 11, lines 25-29, and page 18, Table 2, which shows the results of an ELISA test for demonstrating the specificity of antibodies for *B. anthracis* in comparison and relation to the other species.

The claims have also been revised to emphasize the nature of the EA1 antigen as a polypeptide, as supported by the instant application in Figure 1 and the abstract as well as at page 3, line 13; page 5, lines 22-24; page 6, lines 11-13; page 9, lines 8-14; page 13, lines 26-28; and page 17, line 20. The revisions to claims 16, 19, and 59 are not intended or believed to have altered the scope of the claimed invention, and so no narrowing of the claims is believed to have occurred.

Claims 17-19 have also been revised to substitute the recitation of "incorporates" with the term "comprising". Again, no change in claim scope is intended or believed to have occurred.

Claim 44 has been revised to correspond to revised claim 16.

Claim 54 has been revised to correct a typographical error.

Claim 55 has been canceled in favor of new claims 66-78, which feature a monoclonal antibody that *both* binds the EA1 polypeptide of *B. anthracis and* is specific for the spores or vegetative cells of *B. anthracis*.

Claim 62 has been revised with the re-presentation of subject matter featuring a monoclonal antibody to new claims 79-85.

Claim 63 has been revised with the re-presentation of subject matter from claim 63 to new claim 65.

Claim 64 has been revised to explicitly recite the feature of detecting the complex containing *B. anthracis* as reflecting the detection of *B. anthracis*. Support is found within claim 64 as previously presented.

No new matter has been introduced, and entry of the above revised claims is respectfully requested.

Form PTO-1449

Filed with the instant Reply is a form PTO-1449 listing three documents that are submitted herewith in response to an alleged rejection under 35 U.S.C. §112, second paragraph, as discussed in detail below. Applicants request that the Examiner initial the form after consideration of the documents and return a copy of the initialed form with the next Office Communication to ensure a complete record in the instant application.

Interview of July 12, 2006

Applicants thank Examiner Graser for the courtesy of an in-person interview on July 12, 2006 with co-inventor Beverly Mangold and the undersigned. The Examiner was presented with a brief review of the contents of the Mesnage et al. document of record in comparison with the claims, which features an antibody, or fragment thereof, that *both* binds the EA1 polypeptide of *B. anthracis and* is specific for the spores or vegetative cells of *B. anthracis*.

Initial Remarks

The instant invention is based in part on the discovery that there are epitopes of the EA1 polypeptide that may be used to specifically identify *B. anthracis* apart from other organisms, such as *B. cereus* or *B. thuringiensis*. The discovery was based upon antibodies that bind epitopes found on *B. anthracis* and not on other *Bacillus* species (see for example, paragraphs 0036 to 0039 and Tables 1-4). The epitopes were identified as being present on the

EA1 polypeptide of *B. anthracis*, and so the antibodies are described as binding the EA1 polypeptide.

The invention is not based, however, on the assertion that an antibody which binds the EA1 polypeptide will necessarily be specific to *B. anthracis*. The instant application does not make such an assertion, and the incorrectness of such an assertion is shown by Figure 4 in Mesnage et al., which describes how the EA1 polypeptide of *B. anthracis* is highly homologous to the OlpA polypeptide of *B. licheniformis* over its length (see Figure 4A) and particularly at the N-terminus (see Figure 4B). See also page 1149, last paragraph, in Mesnage et al.

Issues under 35 U.S.C. §112, Second Paragraph

Claims 16-19, 44 and 50-64 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for "mere recitation of a name, i.e., EA1 to describe the invention".

Applicants have carefully reviewed this rejection and respectfully submit that it is misplaced because, as included in the statement of the rejection, the claims are not construed in a vacuum. Instead, the claims are to be read from the perspective of the skilled artisan in the relevant field of technology. That skilled artisan would understand the claims as setting forth the unambiguous identity of the EA1 polypeptide as that of *B. anthracis*.

The skilled person would also be apprised of relevant background information regarding EA1 polypeptide, or protein, from *B. anthracis*. Examples of that information include the enclosed documents by Ezzell Jr. et al., Phillips et al. (abstract only), and Farchaus et al. These documents date from 1988 to 1995 and should be considered in combination with the 1997 Mesnage et al. document. Each of the documents, including Mesnage et al., report in relation to the EA1 antigen, or protein, of *B. anthracis* as a recognized and distinct entity in comparison to other components or parts of *B. anthracis*. Ezzell Jr. et al. report on the use of EA1 antigen to produce an immune response. The Phillips et al. abstract reports on the activities of polyclonal antibodies against EA1 antigen. Importantly, they describe the polyclonal antibodies as cross reactive with both *B. thuringiensis* and *B. cereus*. Farchaus et al. report on

the purification and characterization of the EA1 antigen. And finally, Mesnage et al. report on their characterization of the EA1 antigen and include its amino acid sequence (see Figure 4 therein).

Additional relevant information is found in publicly available deposits of amino acid sequences. The Mesnage et al. EA1 sequence, identified by that name, has been deposited as EMBL CAA68063. EA1 sequences, also identified by that name, from the "Ames ancestor", A2012, and Sterne strains of *B. anthracis* have also been deposited by Read et al., Ravel et al., and Brettin et al. as GenBank AAP24884, ZP_00391261, GenBank AAT29997, and GenBank AAT53169, respectively.

As shown by the documents and deposited sequence information, it is clear that the recognition of a specific protein as the EA1 antigen of *B. anthracis* has been known at least since 1988 and has continued through 1997 to the filing date of the instant application and thereafter. Therefore, and contrary to the instant rejection, is thus no ambiguity in the identity of the EA1 antigen of *B. anthracis*. Accordingly, Applicants respectfully submit that this rejection may be properly withdrawn.

Claims 16, 19, 53, 54, and 59 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. Applicants believe that this rejection has been obviated by the above revisions to the claims, which expressly recite the feature of an antibody, or fragment thereof, that *both* binds the EA1 polypeptide of *B. anthracis and* is specific for the spores or vegetative cells of *B. anthracis*. Accordingly, Applicants respectfully submit that this rejection may be properly withdrawn.

Claims 17-19 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite due to the phrase "which incorporates". Applicants believe that this rejection has been obviated by the above revisions to the claims, which substitute alternative language to express the same intended subject matter and without altering the scope of the claims. Accordingly, Applicants respectfully submit that this rejection may be properly withdrawn.

Claim 54 was rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite due to the presence of two periods. Applicants thank the Examiner for pointing out the typographical error which has been corrected via the above revisions to the claim. Accordingly, Applicants respectfully submit that this rejection may be properly withdrawn.

Claim 62 was rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite due to the inclusion of an "optional" feature. Applicants believe that this rejection has been obviated by the above revisions to the claim, where the monoclonal feature is now presented as subject matter in new claims 79-85. Accordingly, Applicants respectfully submit that this rejection may be properly withdrawn.

Claim 64 was rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite "for omitting essential steps". Applicants believe that this rejection has been obviated by the above revisions to the claim, which now expressly recites the inherent presence of the *B. anthracis* in the formed complex. Accordingly, Applicants respectfully submit that this rejection may be properly withdrawn.

Issues under 35 U.S.C. §112, First Paragraph

Claims 58 and 63 were rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement.

To provide complete deposit information for ATCC deposit PTA-2632, enclosed herewith is a copy of the ATCC deposit receipt for PTA-2632, which was deposited on October 26, 2000 (prior to the April 30, 2001 filing date of the instant application).

As indicated on the receipt, the deposit was made in accordance with the Budapest Treaty and is in compliance with 37 C.F.R. § 1.808(a), such that access to the deposit will be available during the pendency of the patent application making reference to the deposit to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 37 U.S.C. § 122, and all restrictions imposed by the depositor on the availability to the public of the

deposited material will be irrevocably removed, with one exception as set out at 37 C.F.R. § 1.808(b), upon the granting of the patent issuing on the instant application.

In light of the copy of the deposit receipt and the above statement, Applicants believe that the instant rejection may be properly withdrawn.

Issues under 35 U.S.C. §102 and 103(a)

Claims 16, 44, 50-54, and 56-64 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Mesnage et al.

The statement of the rejection includes the assertion that Mesnage et al. disclose "a Western blot assay suggesting that the antibodies were highly specific to B. anthracis and did not cross-react" (see page 7 of the Action mailed April 20, 2006). On the next page, the Action states that "[a]lthough the reference does not specifically recite that the antibody to B. anthracis does not specifically react with B. thuringiensis, it inherently would not since the antigen to which it binds is specific to B. anthracis and the instant specification supports this finding."

Applicants have carefully reviewed the statement of the rejection and the above quoted passages as well as the content of Mesnage et al. and respectfully submit that no *prima facie* case of anticipation has been presented.

Specifically, Mesnage et al. report the production of rabbit **polyclonal** antibodies in sera against the EA1 polypeptide (see page 1154, left column, lower half). There is no description or indication that the polyclonal rabbit antiserum was specific for *B. anthracis* relative to other *Bacillus* species. Instead, Mesnage et al. only discuss specificity (on pages 1150-1151) with respect to the sap protein of *B. anthracis*. There was no comparison to other *Bacillus* species, and the expectation from Mesnage et al. is that the polyclonal antibodies would not be specific relative to other proteins, such as the OlpA protein of *B. licheniformis*.

Mesnage et al. illustrate the degree of similarity and identity between EA1 of *B. anthracis* and OlpA of *B. licheniformis* (see Figure 4 and page 1149, last paragraph, therein as described above). Based on this level of similarity, it would be expected that Mesnage et al. polyclonal antiserum would also react at least with OlpA of *B. licheniformis*. The pending

claims, however, expressly feature an antibody, or fragment thereof, that is specific for the spores or vegetative cells of *B. anthracis* relative to *B. licheniformis*.

Additionally, the Phillips et al. abstract (discussed briefly above and enclosed herewith) expressly report that polyclonal antibodies prepared against gel purified EA1 antigen of *B. anthracis* reacted "with cells of strains of B. cereus and B. thuringiensis". Based on this information, there is no support for the assertion that the polyclonal antibodies of Mesnage et al., also prepared with gel purified EA1 antigen, would have been specific for *B. anthracis* relative to *B. cereus* and *B. thuringiensis*. The pending claims, however, expressly feature an antibody, or fragment thereof, that is specific for the spores or vegetative cells of *B. anthracis* relative to *B. cereus* and *B. thuringiensis*.

Based on the foregoing, Applicants respectfully submit that no *prima facie* case of anticipation exists and the instant rejection may be properly withdrawn.

Issues under 35 U.S.C. §103(a)

Claims 17-19 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Mesnage et al. in view of Loomis et al.

The statement of the rejection includes the assertion that Mesnage et al. teach "that a Western blot assay suggested that the antibodies were highly specific to B. anthracis and did not cross-react. See page 1150-1151". The statement also includes the assertion that it would have been obvious "to use the antibodies taught by Mesnage et al in a colloidal lateral flow detection system as taught by Loomis et al to detect B. anthracis" (see page 13 of the Action mailed April 20, 2006).

Applicants have carefully reviewed the statement of the rejection as well as the content of the cited documents and respectfully submit that no *prima facie* case of obviousness has been presented. As explained by the above review of Mesnage et al., they simply do not teach, suggest, or otherwise indicate an antibody that would be specific for *B. anthracis*. To the contrary, Mesnage et al. seem to suggest or teach that their antibodies would be cross-reactive at least with the OlpA polypeptide of *B. licheniformis*. Additionally, the Phillips et al. abstract

indicates that polyclonal antibodies against EA1 antigen cross react with at least *B. cereus* and *B. thuringiensis*.

In light of these teachings, and contrary to the instant rejection, there is no motivation to use the Mesnage et al. antibodies, which would be expected to cross react with *B. licheniformis*, *B. cereus* and *B. thuringiensis*, to specifically detect *B. anthracis*.

Additionally, there is no expectation of being able to successfully use the Mesnage et al. antibodies to detect *B. anthracis* relative to *B. licheniformis*, *B. cereus* and *B. thuringiensis*.

Given the absence of a motivation to use the Mesnage et al. antibodies in the Loomis et al. system, and the absence of a reasonable expectation of success in specifically detecting *B. anthracis*, Applicants respectfully submit that no *prima facie* case of obviousness is possible, and this rejection may be properly withdrawn.

Claim 55 was rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Mesnage et al. (as applied in the alleged rejection under 35 U.S.C. §102(b) above) in view of Kohler et al. In light of the cancellation of claim 55 in favor of new claims 66-85, Applicants will address this rejection as it may apply to the new claims.

The statement of the rejection includes the assertion that "Kohler et al. teach that making monoclonal antibodies to known antigens was common and have a greater specificity than polyclonal antibodies and can be produced in great quantities" (see page 14 of the Action mailed April 20, 2006). The statement goes on to allege that it would have been obvious that "monoclonal antibodies to the EA1 antigen could be generated/used in place of polyclonal antisera".

Applicants have carefully reviewed the statement of the rejection as well as the content of the cited documents and respectfully submit that no *prima facie* case of obviousness has been presented. It is well known settled that a *prima facie* case of obviousness requires a combination of references that results in the claimed invention. Additionally, a *prima facie* case of obviousness requires a reasonable expectation of success in arriving at the claimed invention. Neither requirement is met in the instant rejection.

The alleged motivation to make monoclonal antibodies against EA1 is based on the advantages reported by Kohler et al. which allegedly would lead to the substitution of polyclonal antibodies with monoclonal antibodies. But such a substitution would not result in the subject matter of claims 66-85 because such a combination of multiple antibodies would still be expected to cross react with other *Bacillus* species. As explained above, Mesnage et al. seem to suggest or teach that their antibodies would be cross-reactive at least with the OlpA polypeptide of *B. licheniformis* while the Phillips et al. abstract expressly indicates that polyclonal antibodies against EA1 antigen cross react with at least *B. cereus* and *B. thuringiensis*. Therefore, and following the logic of the instant rejection, a population of multiple monoclonal antibodies against EA1 of *B. anthracis* would still result in a mixture of monoclonal antibodies that cross react with other species. Thus the antibodies would not be specific as required by the claims.

Additionally, there is no expectation of being able to successfully modify the Mesnage et al. antibodies to produce monoclonal antibodies that are specific for *B. anthracis* and so detect it relative to *B. licheniformis*, *B. cereus* and *B. thuringiensis*. The cross reactivity discussed above would lead the skilled person to expect that there are antigens, like OlpA of *B. licheniformis*, in *B. cereus* and *B. thuringiensis* with high degrees of homology to EA1. The presence of these expected antigens would lead the skilled person to expect that it is unlikely that a monoclonal antibody can be produced to specifically bind *B. anthracis* relative to these other species. Given this low expectation of success, the instant rejection appears to only be supportable by an improper "obvious to try" a combination of the two references to arrive at the claimed invention. The presence of this improper standard prevents the possibility of a *prima facie* case of obviousness.

In light of the above, Applicants respectfully submit that no *prima facie* case of obviousness is possible, and this rejection may be properly withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6151.

Respectfully submitted,

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